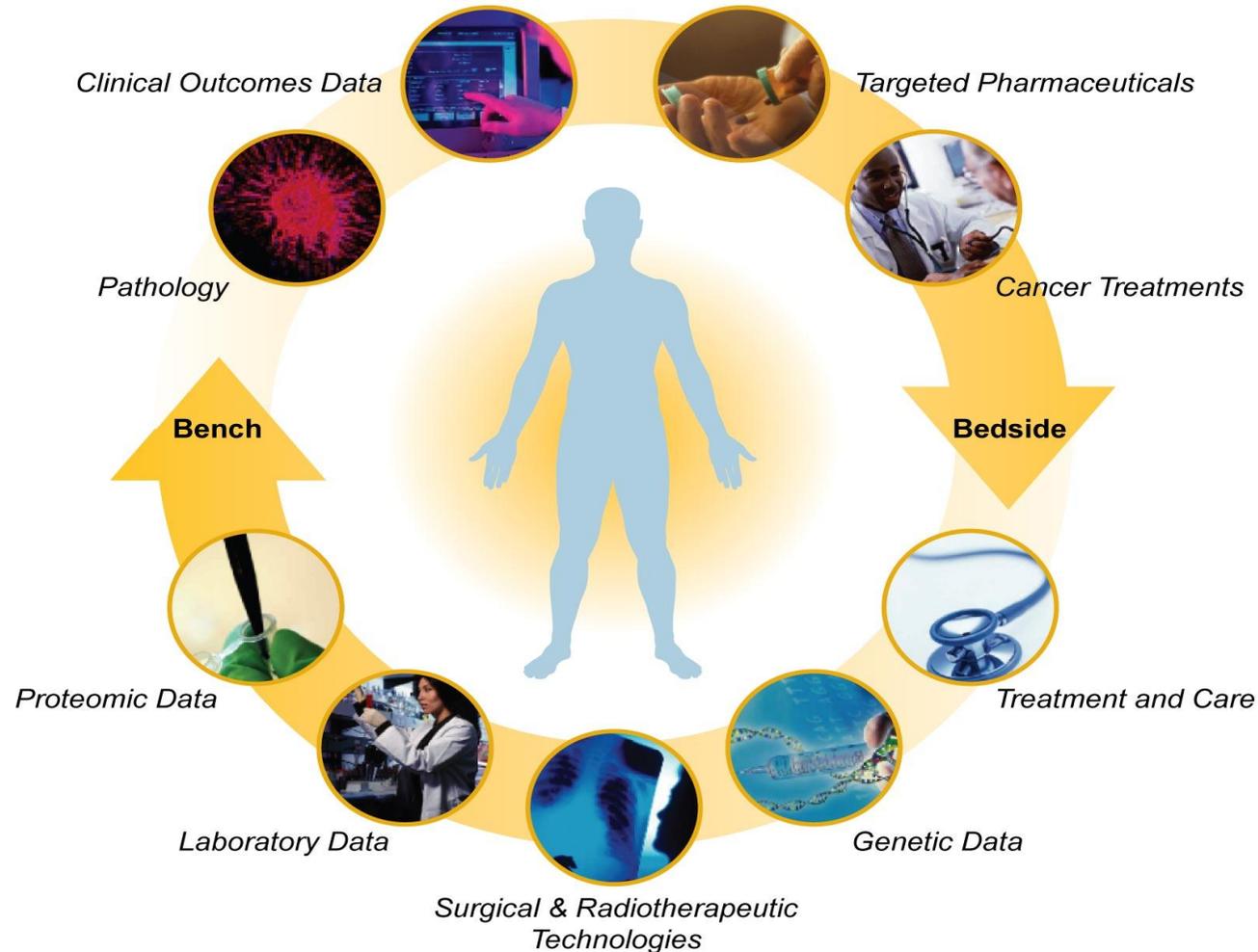


21st Century Medicine: What We're Trying to Achieve



- **Personalized, Predictive, Preemptive, Participatory.....**
- **Unifies clinical research, clinical care, and discovery (bench-bedside-bed) into a seamless continuum**
- **Results in improved clinical outcomes**
- **Accelerates the time from discovery to patient benefit**
- **Enables a health care system, not a disparate “sector”**
- **Empowers consumers in managing their health over a lifetime**

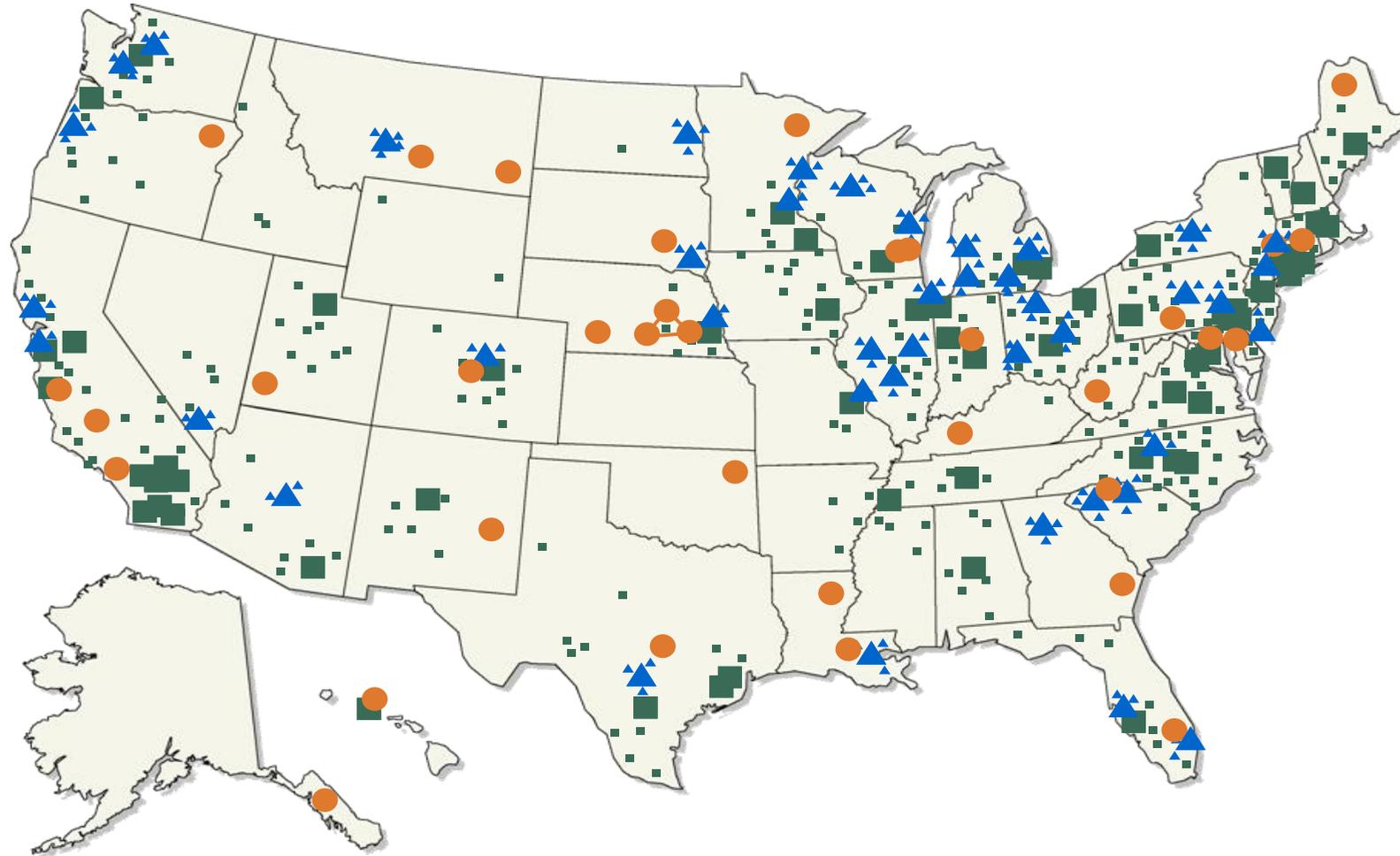
Molecular Medicine as a Complex Continuum



Molecular Medicine



NCI-Designated Cancer Centers, Community Cancer Centers, and Community Oncology Programs



Challenges: The Biomedical Landscape



- Isolated information “islands”
- Information dissemination uses models recognizable to Gutenberg
- Pioneered by Royal Academy of Science of London in the 17th century
 - Write manuscripts
 - “Publish”
 - Exchange information at meetings



The caBIG[®] Initiative



caBIG[®] Goal

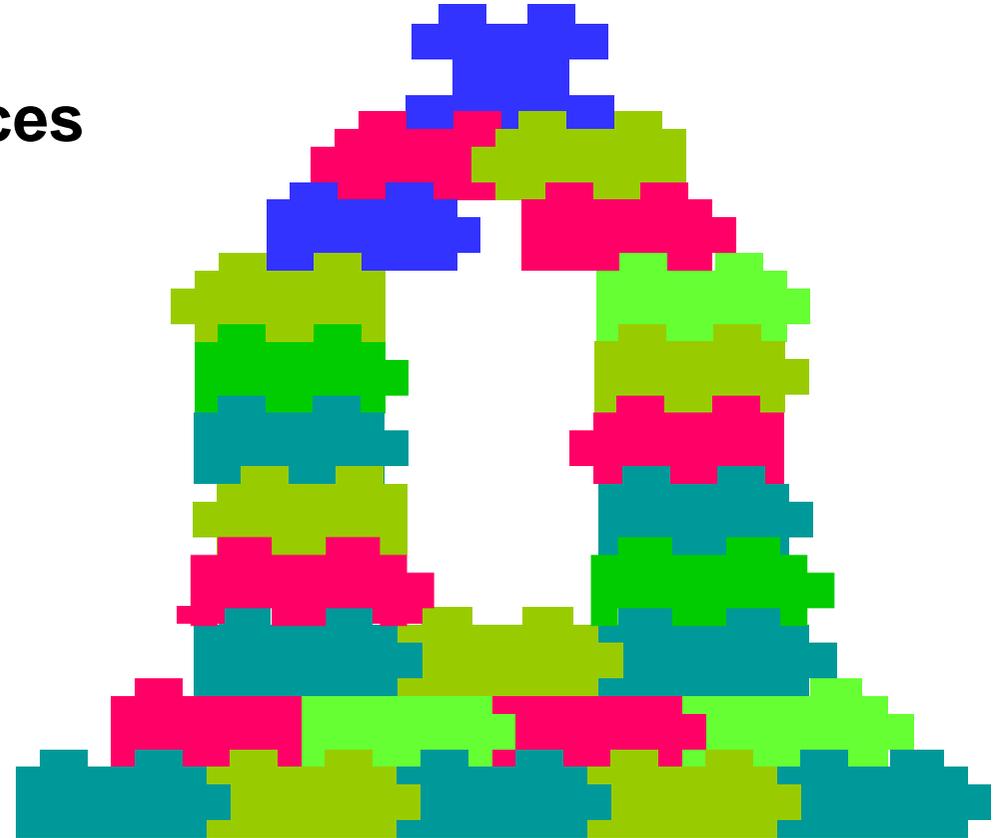
A virtual web of interconnected data, individuals, and organizations that redefines how research is conducted, care is provided, and patients/participants interact with the biomedical enterprise.

caBIG[®] Vision

- **Connect** the cancer research community through a shareable, interoperable infrastructure
- **Deploy and extend** standard rules and a common language to more easily share information
- **Build** or adapt tools for collecting, analyzing, integrating and disseminating information associated with cancer research and care



- **Modules that address specific needs**
- **Connect through defined Electronic interfaces**
- **Use of international data standards**



caBIG[®] Capabilities Enable Discovery > Clinical Research > Clinical Care



Molecular Medicine



Clinical Research



Imaging



Molecular Biology



Pathology

caBIG[®] Capabilities Enable Discovery > Clinical Research > Clinical Care



- Track clinical trial registrations
- Facilitate automatic capture of clinical laboratory data
- Manage reports describing adverse events during clinical trials



Clinical Research

Molecular Medicine



Imaging

- Utilize the National Cancer Imaging Archive repository for medical images including CAT scans and MRIs
- Visualize images using DICOM-compliant tools
- Annotated Images with distributed tools

- Combine proteomics, gene expression, and other basic research data
- Submit and annotate microarray data
- Integrate microarray data from multiple manufacturers and permit analysis and visualization of data



Molecular Biology



Pathology

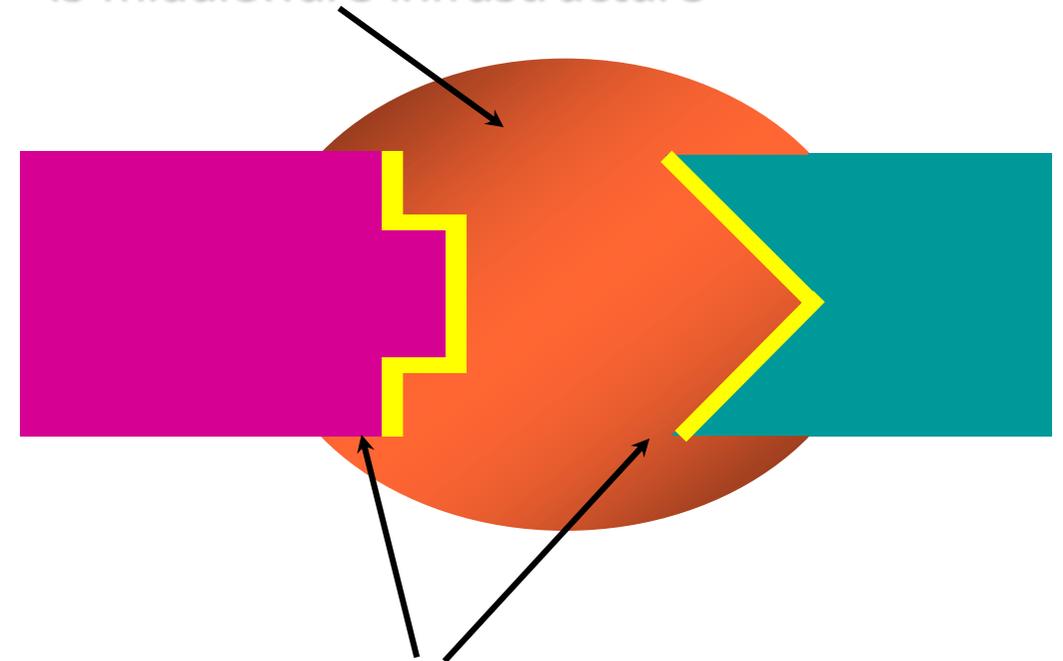
- Access a library of well characterized, clinically annotated biospecimens
- Use tools to keep an inventory of a user's own samples
- Track the storage, distribution, and quality assurance of specimens

Boundaries and Interfaces



- **Focus on boundaries and interfaces, how things fit together, not on the internal details**
- **Once they're built: assume that will be diverse & changing**

The glue that binds parts together is middleware infrastructure

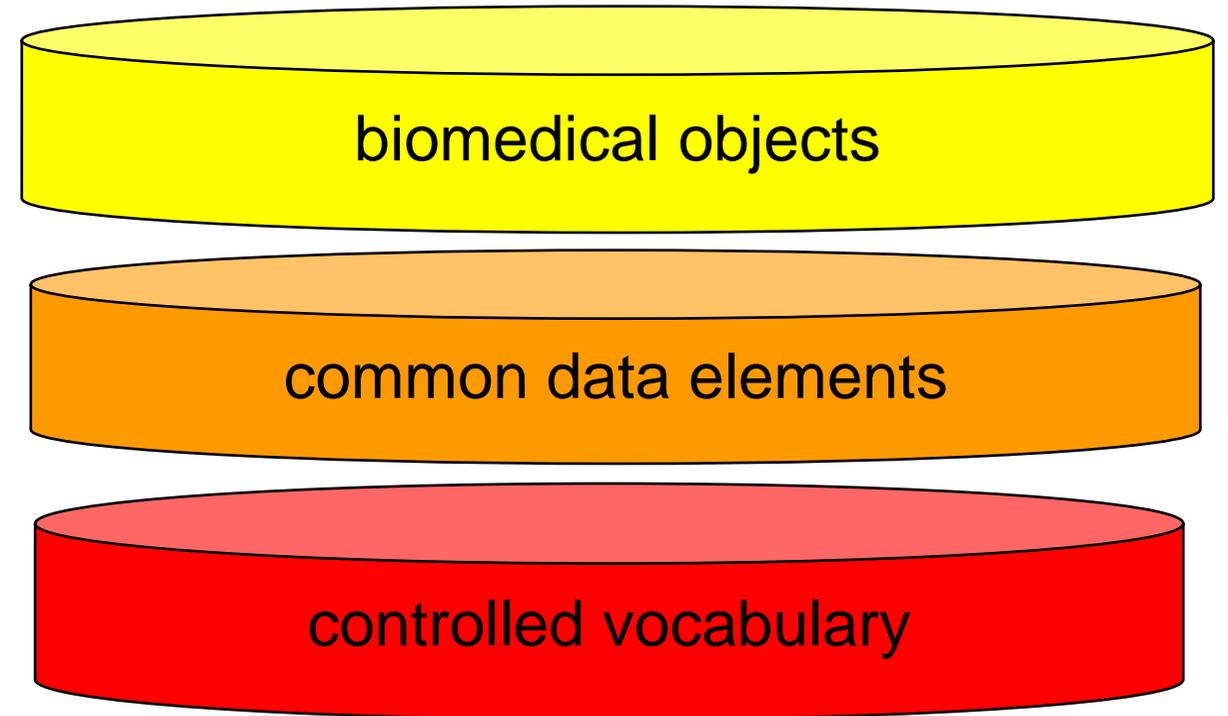


Shape of boundary is defined in APIs

Standards-Based Interoperability: caCORE



- **Community driven**
- **Dynamic implementation**
 - Built to be upgraded as standards “harden”, and domains expand



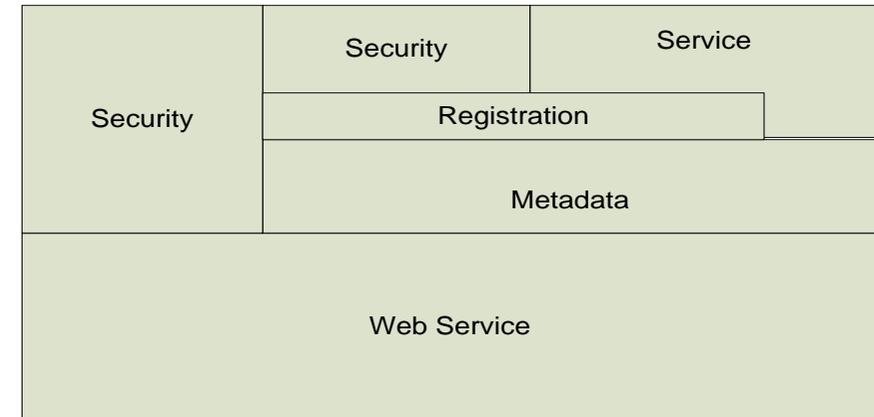
Standards Based Technical Infrastructure



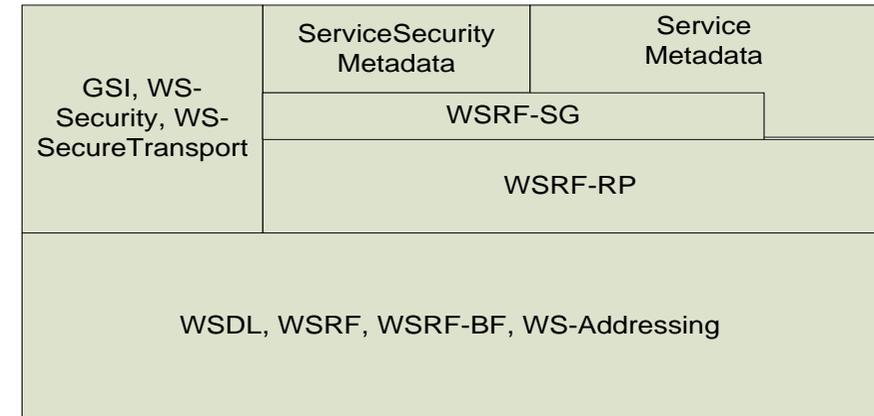
Grid Services

- **caGrid uses the Globus Toolkit and Axis for creating, registering, discovering, and invoking these service operations as grid services**
- **Client uses the operation through a grid service interface and does not need to be aware of any implementation specific details of the grid service**

Service Layers



Layer Specifications



Service Layers



Web Server (Apache/Tomcat): Binds to server port(s)

Web Application Server (Tomcat): Hosts web applications connected to the web server

SOAP Engine (Axis): Interprets SOAP requests, installed as a web application

Web/Grid Service (Globus): Binds "protocol" to operations on local application resources

Security (GSI)

- * Secure Communication
- * Authentication
- * Authorization

Metadata (WSRF – Resource Properties)

- * caGrid Service Metadata
- * caGrid Service Security Metadata
- * (caGrid Data Service Metadata)
- * (Custom Metadata)

Service Definitions

- * WSDL
- * XSDs

Service Implementation

Advertisement
(WSRF-SG)

Configuration
Properties

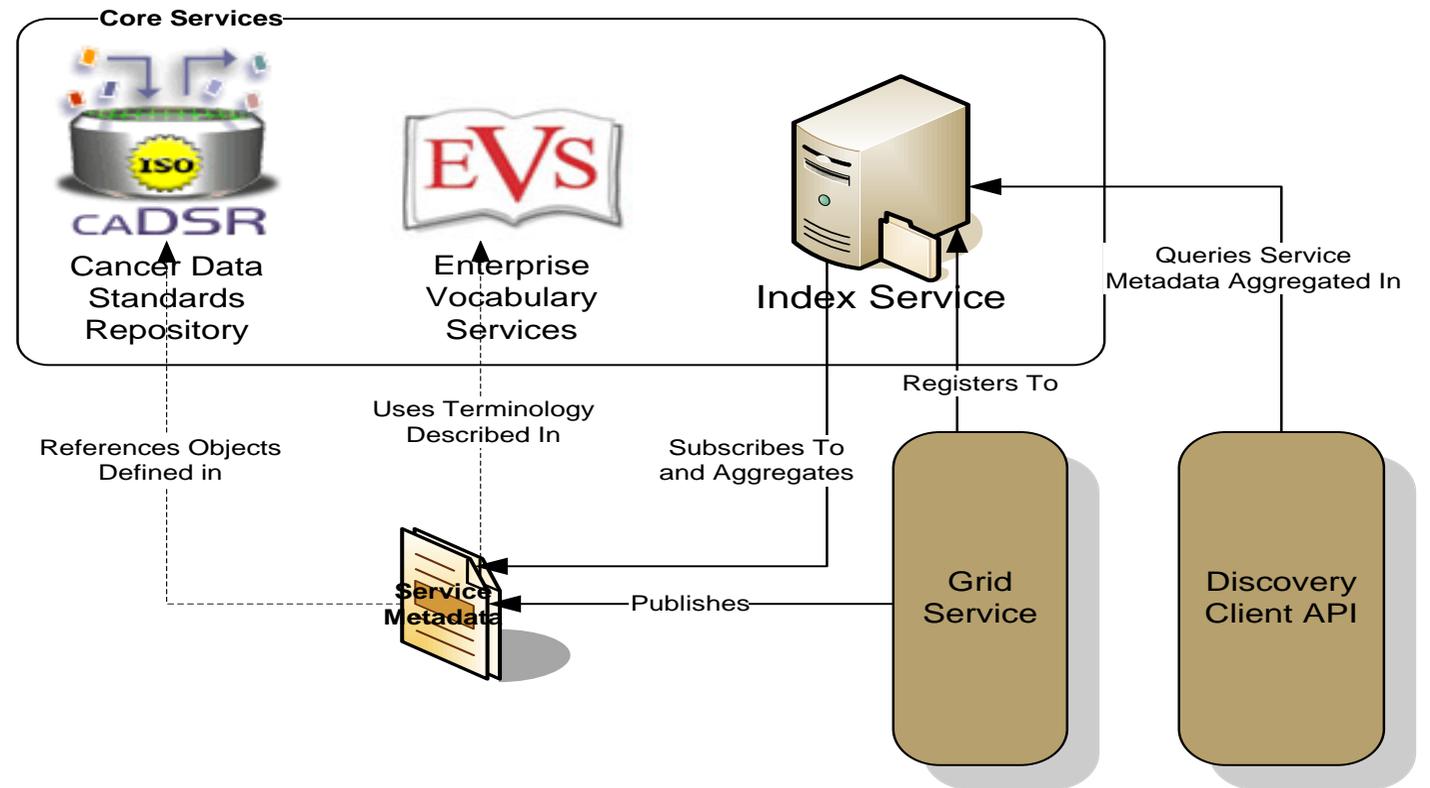
Business Logic

Resources
(WSRF
Resource)

Advertisement and Discovery Process



- All services register their service location and metadata information to an Index Service
- The Index Service subscribes to the standardized metadata and aggregates their contents
- Clients can discover services using a discovery API which facilitates inspection of data types
- Leveraging semantic information in EVS (from which service metadata is drawn), services can be discovered by the semantics of their data types

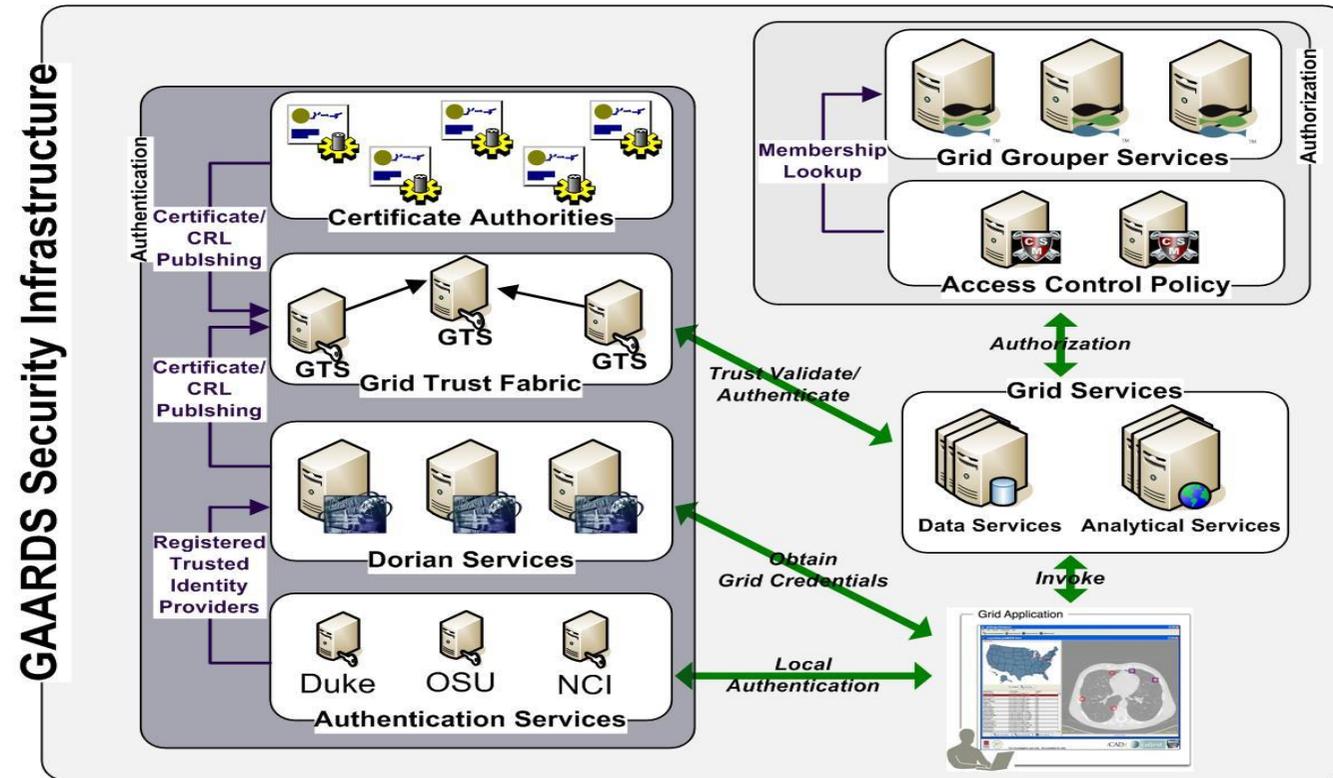


caGrid Security Infrastructure (GAARDS)



GAARDS provides services and tools for the administration and enforcement of security policy in an enterprise Grid.

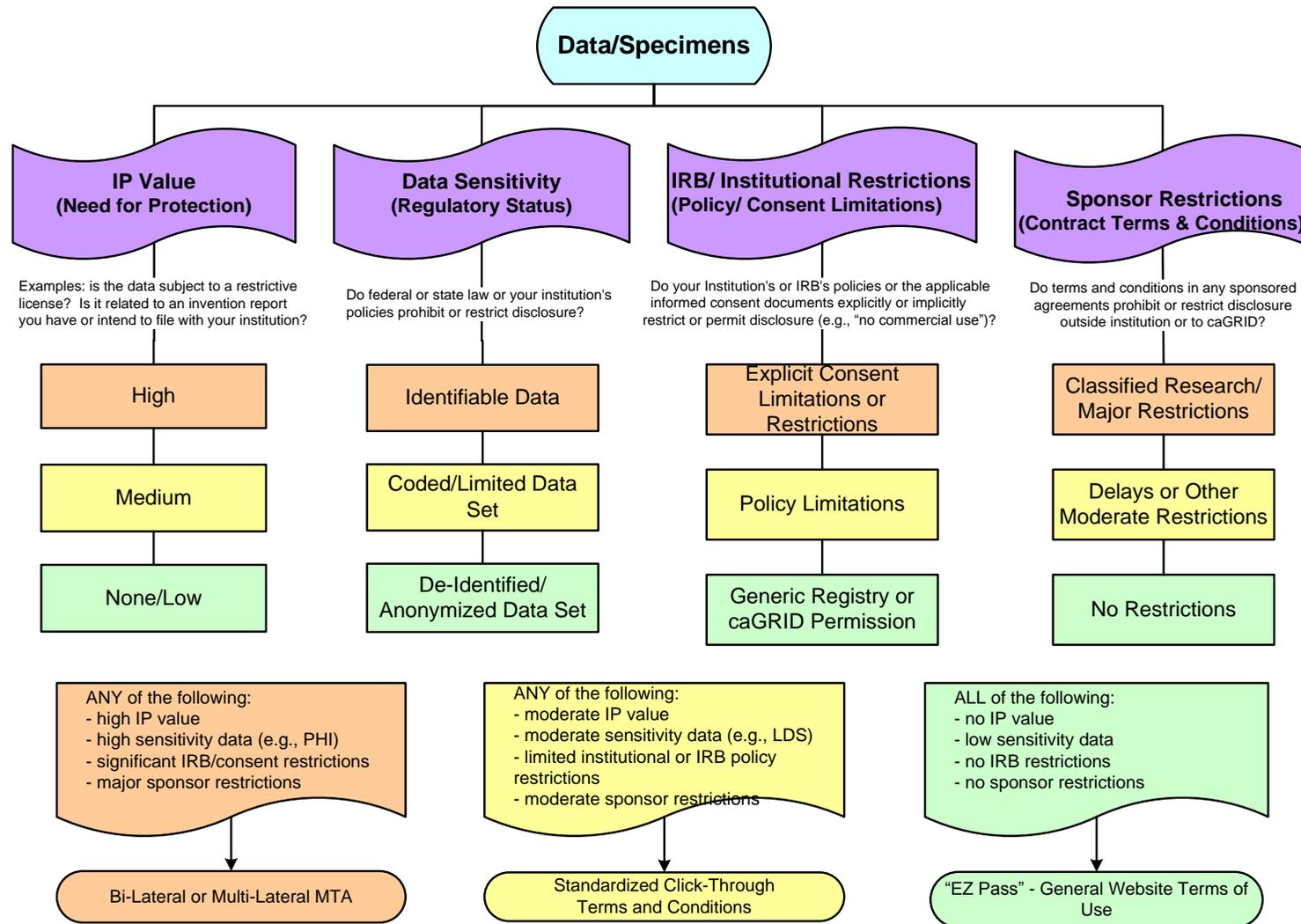
- **Dorian**
 - Grid Account Management
 - Allows accounts managed in external domains to be federated and managed in the grid.
 - Dorian allows users to use their existing credentials (external to the grid) to authenticate to the grid
 - Issues Host Certificates.
- **Grid Trust Service (GTS)**
 - Creation and Management of a federated trust fabric.
 - Supports applications and services in deciding whether or not signers of digital credentials can be trusted.
 - Supports the provisioning of trusted certificate authorities and corresponding CRLs.



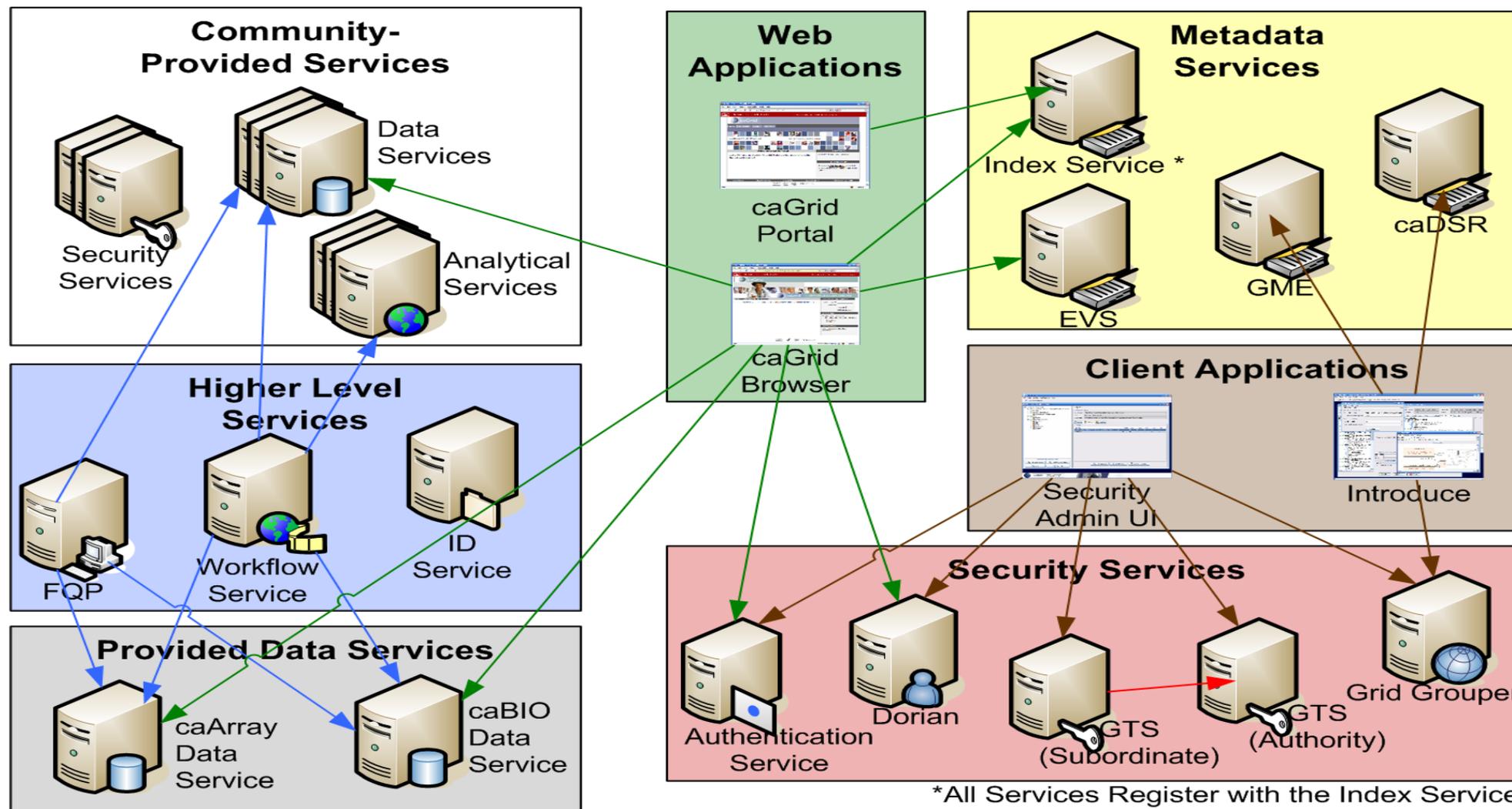
Policy: Analysis Framework



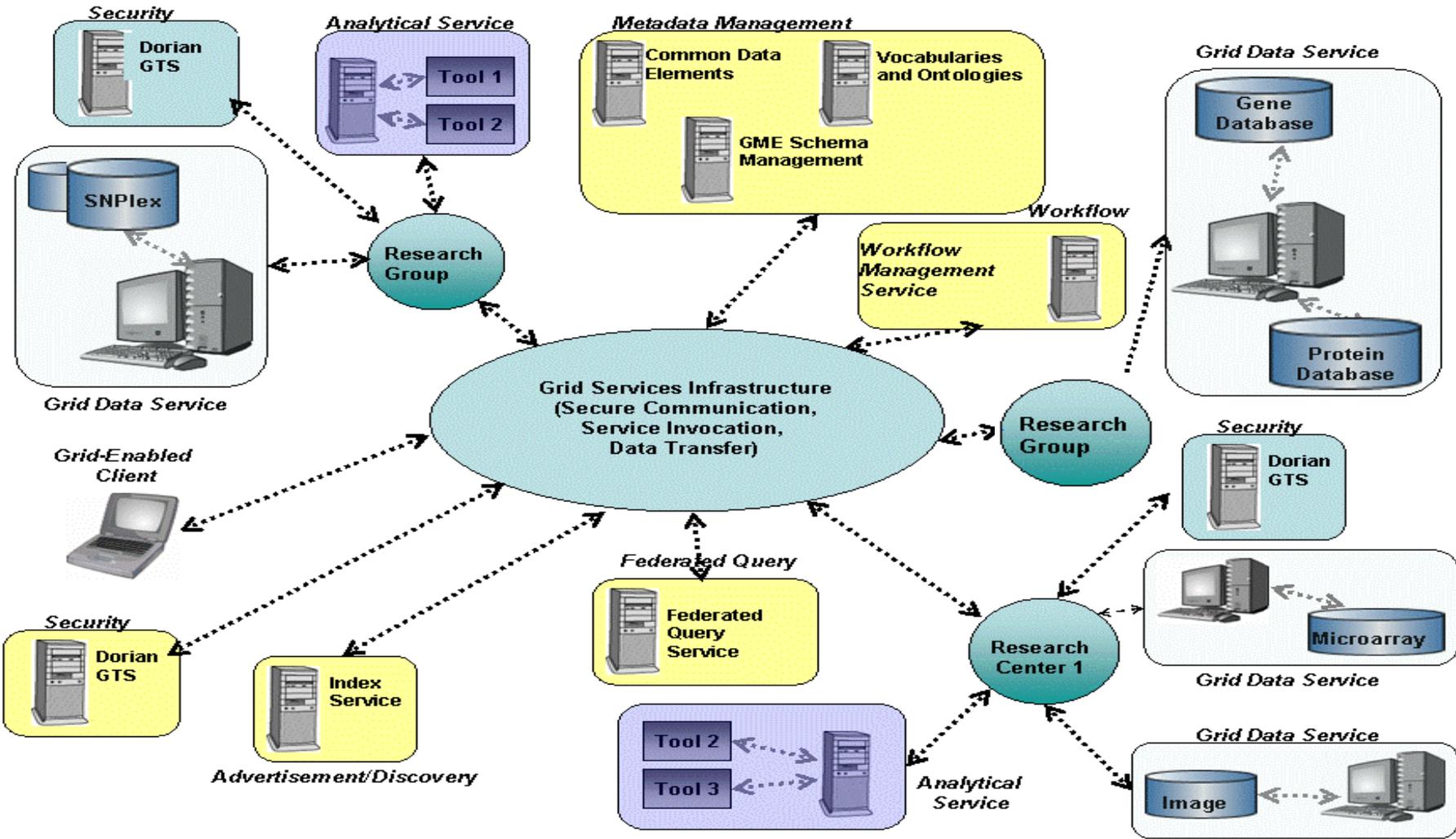
Decision Tree for Privacy/Intellectual Capital Terms and Conditions



caGrid Production Environment



caGrid Conceptual View

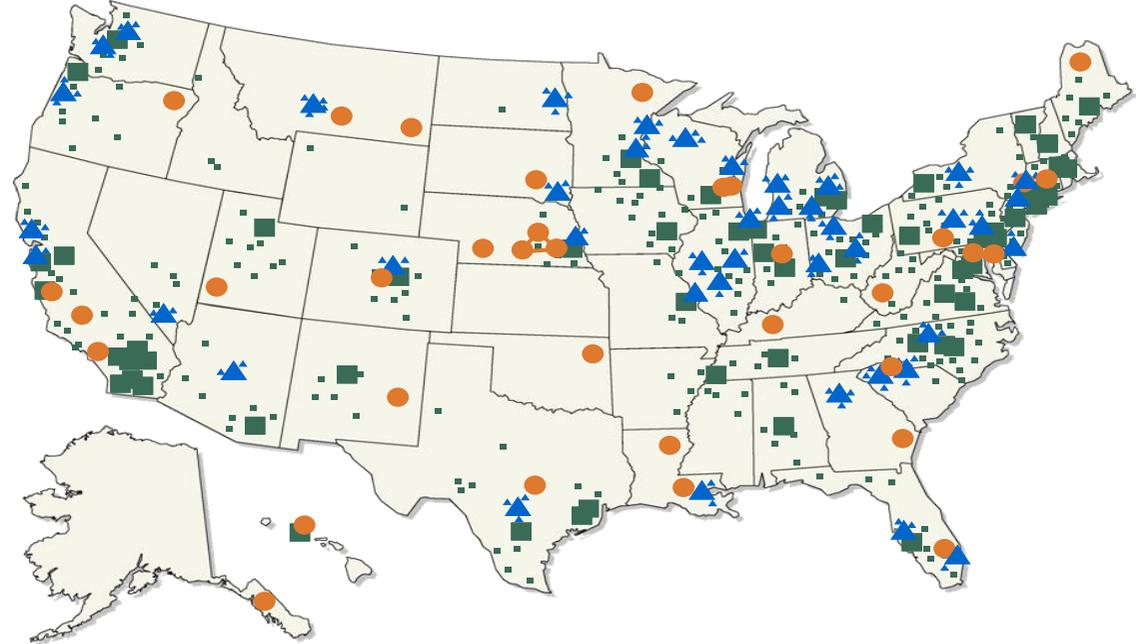


Connected with caBIG[®]



- **caBIG[®] adoption is unfolding in:**
 - 56 NCI-designated Cancer Centers
 - 16 NCI Community Cancer Centers
- caBIG[®] being integrated into federal health architecture to connect **National Health Information Network**
- **Global Expansion**
 - United Kingdom
 - China
 - India
 - Latin America

NCI-Designated Cancer Centers, Community Cancer Centers, and Community Oncology Programs



caBIG[®] Snapshot



caBIG :: caGrid Portal - Mozilla Firefox

File Edit View History Bookmarks Tools Help

http://cagrid-portal.nci.nih.gov/web/guest/home

Wikipedia (en)

National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

caGrid Portal Welcome!

HOME SERVICES TOOLS NEWS REGISTER caBIG

Log In | Register

News

Subscribe to caGrid News Feed

caGrid Portal 2.0.2 Released
[Jun 16, 2008 4:39:34 PM]
caGrid Portal 2.0.2 has been released

caGrid makes list of top open source tools.
[May 16, 2008 4:39:34 PM]

caGrid Links

[caGrid Portal Users Guide](#)
[caGrid Portal Wiki Pages](#)
[caBIG Community Website](#)
[caGrid Website](#)
[caGrid Wiki](#)

Gateway to the cancer Biomedical Informatics Grid.

caGrid Portal provides a visual display of the services that are running on the caGrid infrastructure and also institutions that are participating in the caBIG program. Click on the map icons below to link to details about caGrid services and caBIG participants. You can also select categories of items to be viewed on the map.

From the **Services** tab, you can find caBIG services, participants, and points of contact. There, you can also query caGrid data services, share your queries, and search for queries of other community members.

From the **Tools** tab, you can find all the caBIG software tools, database technologies and web-based applications

Categories: ----

- Data Service
- Analytical Service
- Participant Institute
- Hosting Research Center
- Point of Contact

POWERED BY Google

Map data ©2008 Tele Atlas, Europa Technologies - [Terms of Use](#)

caGrid Status

Here are the five newest services...

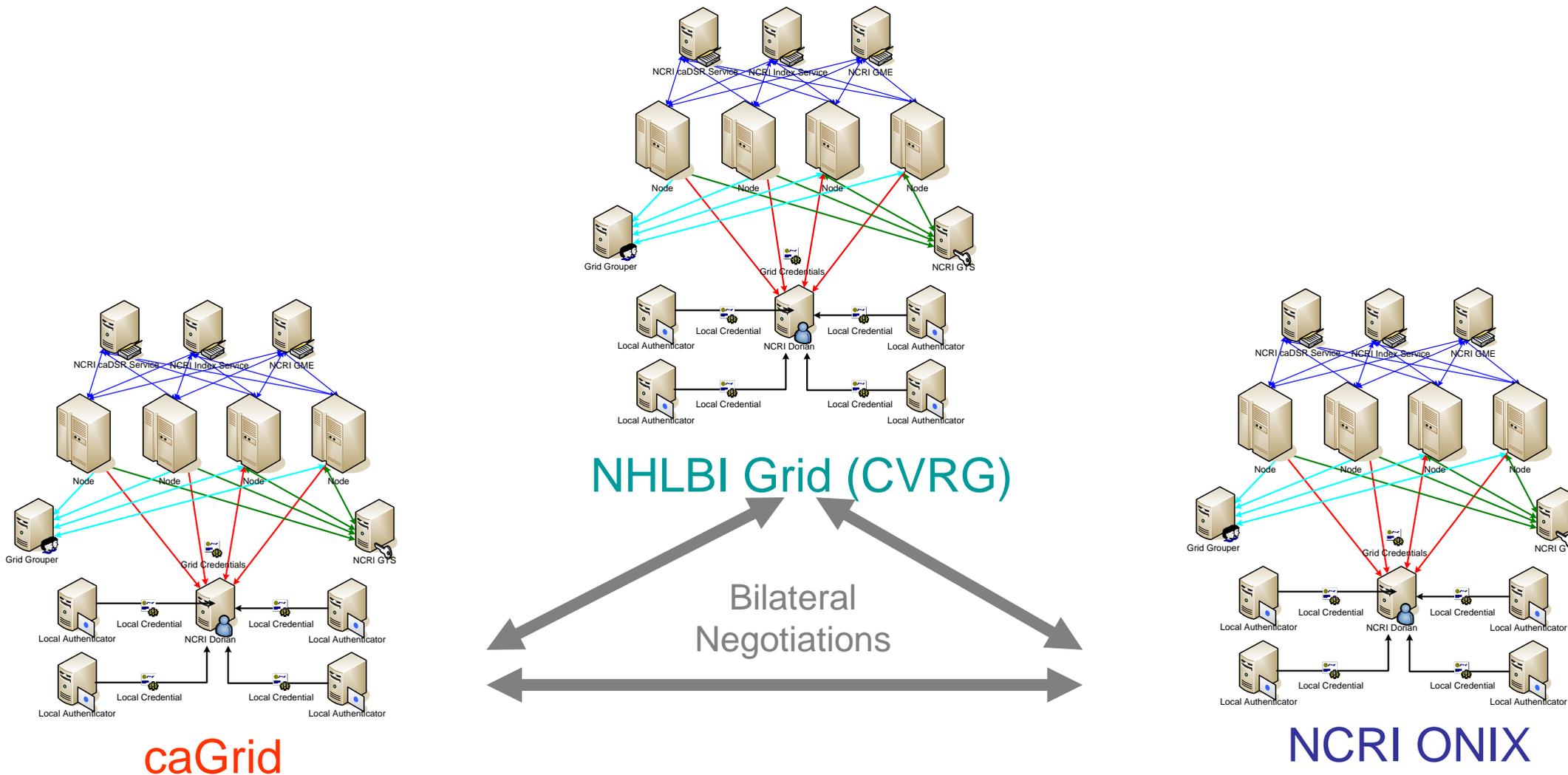
Name	Type
CaArraySvc	
CaTissueCore	
CaArraySvc	
PreprocessData..	
CaersDataServ..	

There are currently...
122 caBIG Participants,
99 grid services, which include
72 data services, and
27 analytical services.

Last Updated: 1 minute ago

Done

Grid of Grids...



caBIG[®] - The Next Wave:

Reaching End Users



caBIG[®] Installation Support

- A software packaged to facilitate installation including on-line Tutorials and Videos and Learning Center materials

Knowledge Centers – Power to the People

- A one-stop shop for domain expertise, technical and end-user documentation, training materials, and comprehensive, up-to-date installation packages for caBIG[®] tools
- A centralized site providing administration of open source development of caBIG[®] tools, collection and monitoring of defect reports, feature requests, and end-user requirements

Licensed Support Service Providers – Helping Hands

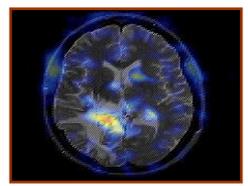
- Organizations that provide hands-on deployment support, customization, help desk, documentation development and end-user training



Connecting multiple sources, experiments, and data types

Three forms of cancer

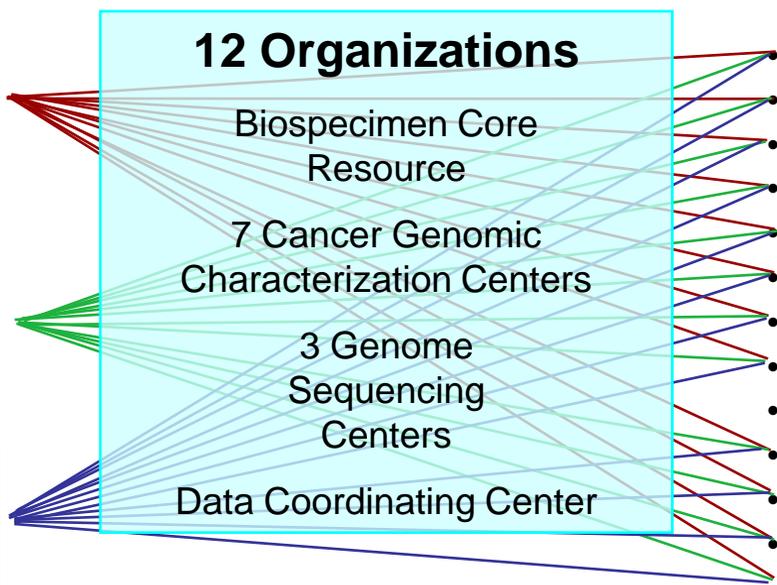
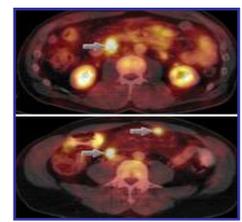
glioblastoma multiforme
(brain)



squamous carcinoma
(lung)

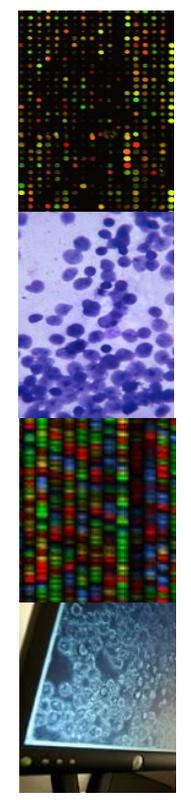


serous
cystadenocarcinoma
(ovarian)



Multiple data types

- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic status
- Tissue anatomic site
- Surgical history
- Gene expression
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence





Empowering researchers to integrate increasingly complex layers of cancer biology, from gene to clinical phenotype, as a whole



All from their computer

A single web-based portal for all analyses – <http://cma.nci.nih.gov>



caBIG™ cancer Biomedical Informatics Grid™

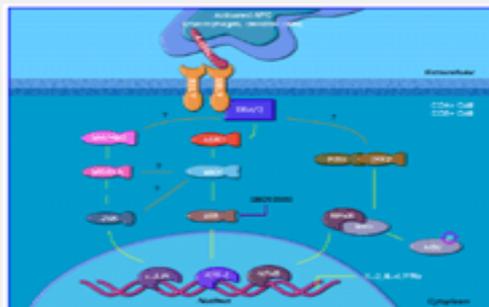
Cancer Molecular Analysis Portal

Gene View

Gene View

Visualize gene expression, copy number, SNP, and pathway data on a gene by gene basis. Generate detailed study related reports for a given gene.

Available resources include: Gene Expression Plots, KM Survival Plots, CGWB Integration, and Pathway Visualizations.



Genome View

Clinical View

Analysis Tools

Existing Users:

user:
pass:

Additional Information:

- ◆ Register
- ◆ Provide your feedback

A single web-based portal for all analyses – <http://cma.nci.nih.gov>



caBIG™ cancer Biomedical Informatics Grid™

Cancer Molecular Analysis Portal

Gene View

Genome View

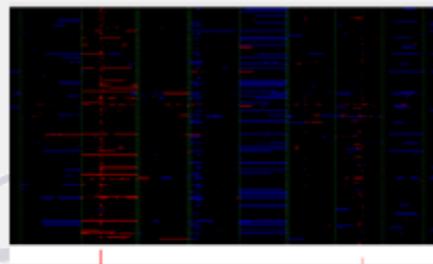
Clinical View

Analysis Tools

Genome View

Explore all of the study data in one genome level visualization. Investigate chromosomal regions of amplification, deletion and over expression. Zoom in on a chromosomal region of interest for a more detailed view.

Available resources include: Integrated Heatmap Viewer for Genomic Data.



Existing Users:

user:

pass:

Additional Information:

- ◆ [Register](#)
- ◆ [Provide your feedback](#)

A single web-based portal for all analyses – <http://cma.nci.nih.gov>



caBIG™ cancer Biomedical Informatics Grid™

Cancer Molecular Analysis Portal

Gene View

Genome View

Clinical View

Analysis Tools

Clinical View

Investigate the study clinical data. Explore the relationships between clinical and molecular study data.

Available resources include: Clinical Query with Reports and KM Sample Plots



Study	Sample ID	Sample Type	Sample Status	Sample Date	Sample Location	Sample Description
NCI-1000	NCI-1000-001	Primary Tumor	Available	2007-01-01	NCI-1000	Primary Tumor
NCI-1000	NCI-1000-002	Primary Tumor	Available	2007-01-01	NCI-1000	Primary Tumor
NCI-1000	NCI-1000-003	Primary Tumor	Available	2007-01-01	NCI-1000	Primary Tumor
NCI-1000	NCI-1000-004	Primary Tumor	Available	2007-01-01	NCI-1000	Primary Tumor
NCI-1000	NCI-1000-005	Primary Tumor	Available	2007-01-01	NCI-1000	Primary Tumor



Existing Users:

user:

pass:

Additional Information:

- ◆ Register
- ◆ Provide your feedback

A single web-based portal for all analyses – <http://cma.nci.nih.gov>



National Cancer Institute

Context: TCGA



caBIG™ cancer Biomedical Informatics Grid™

Cancer Molecular Analysis Portal

Gene View

Genome View

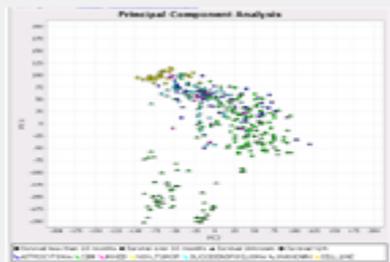
Clinical View

Analysis Tools

Analysis Tools

Analyze the study data using analysis tools such as Genepattern, Principal Component Analysis, and the Cancer Genome Workbench

Available resources include: PCA Analysis and Gene Pattern Integration



Existing Users:

user:
pass:

Additional Information:

- ◆ Register
- ◆ Provide your feedback



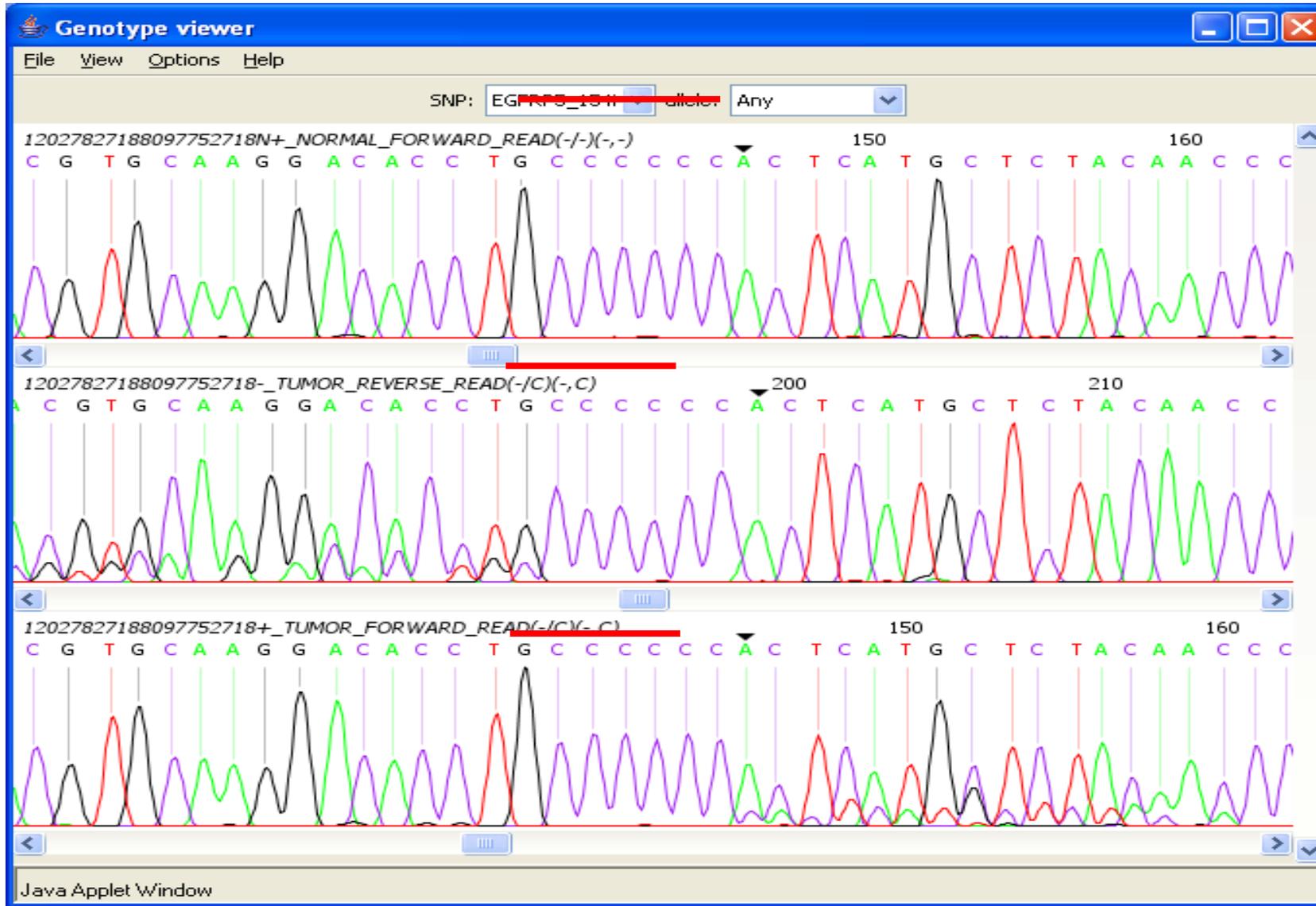
FIRSTGOV

Comprehensive Summary



Putative Somatic Mutations Can Be Manually Reviewed

Example: A frameshift mutation in EGFR in paired tumor/normal



Normal

Tumor

Protein Structure View of EGFR Mutations



Protein Structure 3D viewer - Mozilla Firefox

File Edit View History Bookmarks Tools Help

https://cgwb.nci.nih.gov/cgi-bin/3dViewer/Gene.cgi?proj=valid&sym=EGFR

Human chr7:55,053,218-55,243,524 - ... Protein Structure 3D viewer

National Cancer Institute
Protein Structure Viewer
Gene : EGFR GI : 29725609 1210 aa Also see GI : 41327736 41327732 41327734

Access proteins from alternative splicing

Protein Motifs : 4 Pdb hits: 1
SNP LogE & SIFT: Red : Predicted Deleterious Blue : Predicted Tolerant Black : Undecided Gray : Not Analyzed
Phosphorylate : 29 Pubmed Tabular format

1 1000 1200

Click to get 3D viewer

Done cgwb.nci.nih.gov

3D Structure Viewer



Big, highlighted atoms refer to the mutated amino acids (shown in red in the bottom panel). You can also click on the mutated amino acid (shown in red) to turn on or off a specific mutation

Protein Structure 3D Viewer - Mozilla Firefox

https://cgwb.nci.nih.gov/cgi-bin/3dViewer/ViewAA.cgi?proj=valid&gi=29725609&id=722&pdb=1yy9:A&sim=0.995&gstart=25&glen=613&phos=

National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

GI: 29725609 Viewing region 25 - 638 99.5 % similar to Pdb: 1yy9 chain A 2 - 614

1yy9

Jmol

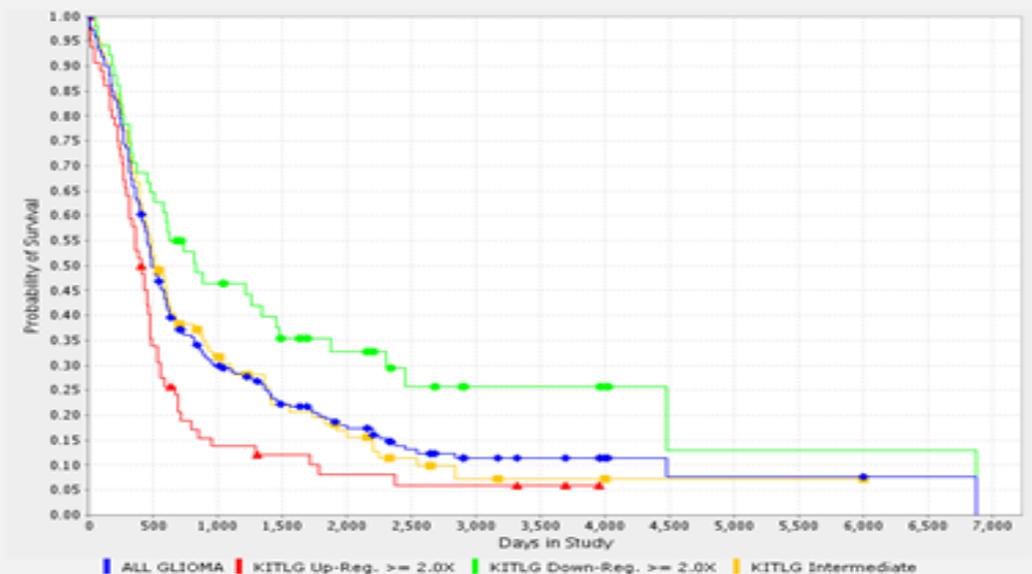
start	Sequence : Click on a letter once will turn on the spacefill. Double-click on the same letter will turn the spacefill off.	end
2	EEKKVCQGTSNKLTLQLGTFEDHFLSLQRMFNCEVVLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNT	71
72	VERIPLLENLQIIRGNMYYENSIALAVLSNYDANKTGLKELPMRNLQEIILHGAVRFSNNPALCNVESIQWRD	142
143	IVSSDPLSNMSMDFQNHLSGCQKCDPSCPNGSCWGAAGEENCQKLTKIICAQCCSGRCRGRKSPSDCCCHNQCA	213
214	AGCTGRRESDCLVCRKFRDEATCKDTCPPMLLYNPTTYQMDVNPPEGKYSFGATCVKCKPRNYVVTDHGSCV	284
285	RACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGEFKDSLSINATNIKHFKNCTSSISGDLHILPVAFRGD	355
356	SFTHTPPLDPQELDILKTVKEITGFLLIQAWPENRTDLHAFENLEIIRGRTKQHGGQFSLAVVSLNITSLGL	426
427	RSLSKEISDGDVVISGNKNLCYANTINWKKLFGTSGQKTKIISNRGENKCKATGQVCHALCSPEGCWGPPEPR	497
498	DCVSCRNVSRGRECVDKCKLLEGEPRFVENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCV	568
569	KTCPAGVMGENNTLVWKYADAGHVCHLCHPNCTYGGCTGPGRLRGCP	614

Jmol script completed cgwb.nci.nih.gov

Gene Expression Analyses Related to Clinical Outcome



Kaplan-Meier Survival Plot for Samples with Differential KITLG Gene Expression



[Upregulating Samples](#) [View Clinical Reports](#) [Downregulating samples](#) [Intermediate Samples](#)

Statistical Report:

KITLG
Reporter: 211124_s_at

Number of samples in group:

Up-Regulated	64
Down-Regulated	51
Intermediate:	96

Log-rank p-value (for significance of difference of survival between group of samples)

Up-Regulated vs. Intermediate:	0.0257
Up-Regulated vs. Down-Regulated	2.0E-4
Down-Regulated vs. Intermediate:	0.0022



Administration:

- ◆ [View Results](#)
- ◆ [List Management](#)
- ◆ [Help](#)

News:

- ◆ **Data Version**
- ◆ TCGA newsletter - March 2008
- ◆ Number of Patients - 110
- ◆ Number of Expression Arrays - 985
- ◆ Number of Copy Number Arrays - 361

PatientDID Lists:

- ◆ ALL_PATIENTS
- ◆ Low_Survival
- ◆ Med_Survival
- ◆ High_Survival
- ◆ TP53_SomaticMut...
- ◆ EGFR_SomaticMut...
- ◆ PTEN_SomaticMut...
- ◆ RB1_SomaticMut...
- ◆ DST_SomaticMut...
- ◆ NF1_SomaticMut...
- ◆ CDKN2A_Somatic...
- ◆ PIK3R1_Somatic...
- ◆ CENPF_SomaticM...
- ◆ ITGB3_SomaticM...

Gene Lists:

- ◆ TCGA Target Se...

Reporter Lists:

High Order Analyses: Pathways



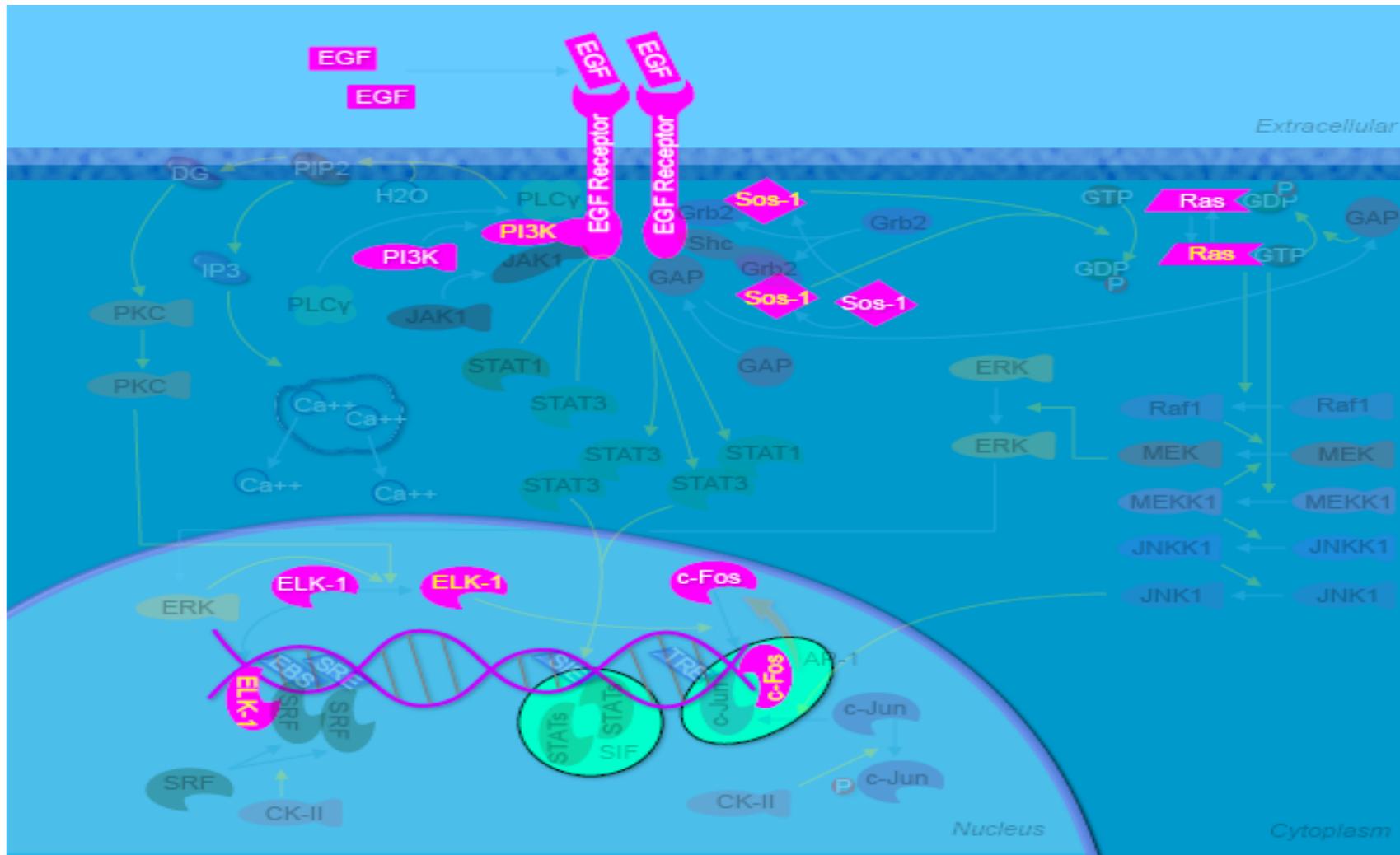
Pathways and Associated Anomalies

⏪ ⏴ ⏵ ⏩ | 100 ▾
 First Prev Next Last Rows Displayed

309 results found, displaying 1 to 100

Pathway	Any Anomaly/Agent	Mutated	Amplified	Deleted	Agents
ADP-Ribosylation Factor	●		●		
AKAP95 Role in Mitosis and Chromosome Dynamics					
AKT Signaling Pathway					
ALK in Cardiac Myocytes	●				●
ATM Signaling Pathway	●	●			●
Acetylation and Deacetylation of RelA in Nucleus					
Actions of Nitric Oxide in the Heart					
Activation of CSK Inhibits Signaling through the T Cell Receptor	●		●		●
Activation of PKC through G-Protein Coupled Receptors					
Activation of cAMP-dependent Protein Kinase, PKA	●		●		
Acute Myocardial Infarction	●			●	
Adhesion Molecules on Lymphocyte					
Adhesion and Diapedesis of Granulocytes					
Adhesion and Diapedesis of Lymphocytes	●				●
Aqrin in Postsynaptic Differentiation	●	●	●	●	
AhR Signal Transduction Pathway					
Alpha-synuclein and Parkin-mediated Proteolysis in Parkinson's Disease					
Alternative Complement Pathway	●				●
Angiotensin II Mediated Activation of JNK Pathway via Pyk2 Dependent Signaling	●	●	●		

EGFR Network Mutation Profile Through CMA



A Systems Approach: BIG Health Consortium™

“The world we have created today has problems which cannot be solved by thinking the way we thought when we created them.”*

**Albert Einstein*

Vision:

A biomedical system that synergizes the capabilities of the entire community to realize the promise of personalized medicine

Mission:

The BIG Health Consortium™ is a collaboration among stakeholders in biomedicine, including **government, academe, industry, non-profit, and consumers**, who come together in a novel organizational framework **to demonstrate the feasibility and benefits of the personalized medicine paradigm.**

Strategy:

Through a series of personalized medicine **demonstration projects**, with an expanding number of collaborators, BIG Health will **bootstrap** a new approach in which clinical care, clinical research, and scientific discovery are linked.

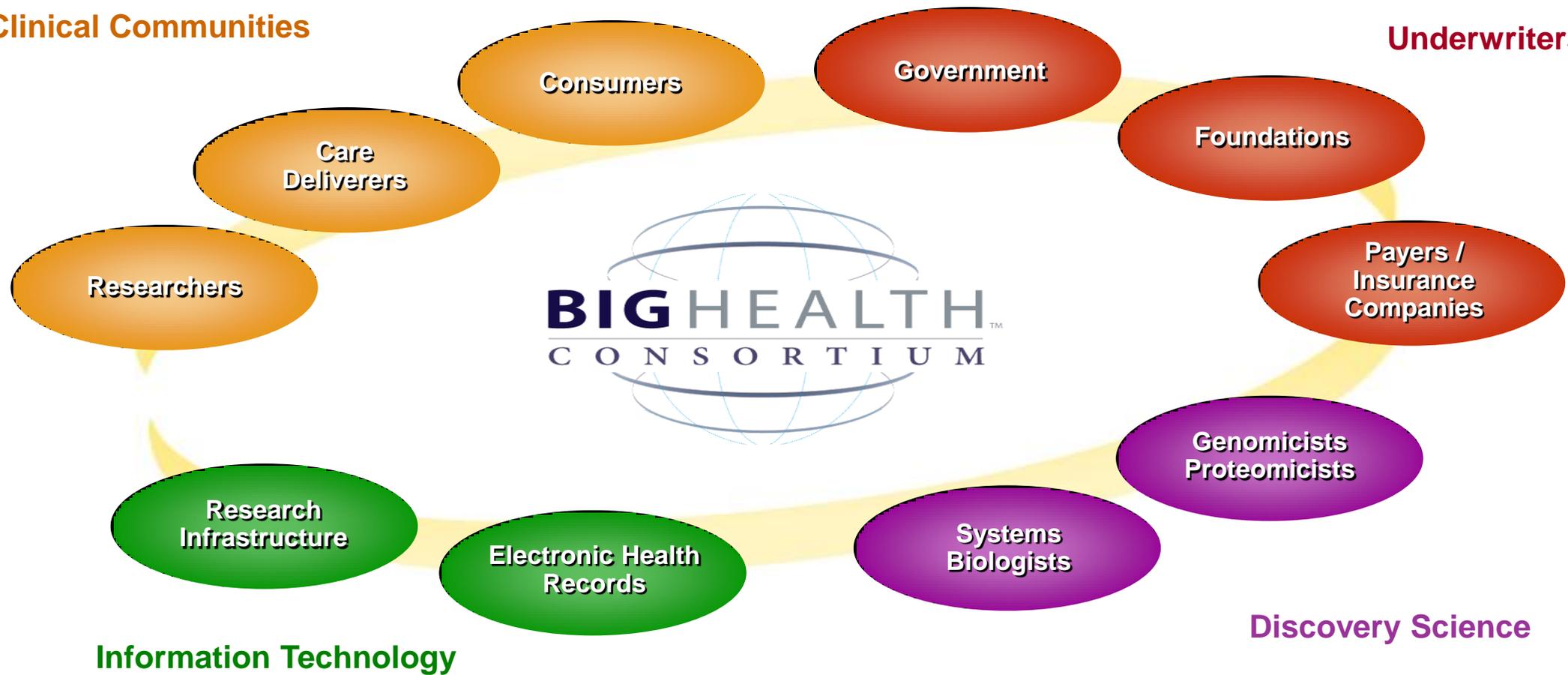
BIG Health will demonstrate that:

- Loosely-coupled sectors within life sciences and health care can come together in an ecosystem to implement personalized medicine real-world projects, in real time.
- The tools, infrastructure and standards of NCI's informatics infrastructure (caBIG[®]) can be applied to linking this ecosystem.
- Such an ecosystem can be financially self-sustaining.
- ***Clinical care, clinical research, and scientific discovery can be connected in a seamless continuum that speeds innovation and benefits patients.***

BIG Health Ecosystem

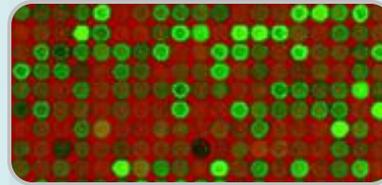
Clinical Communities

Underwriters





Research



BCM
Baylor College of Medicine

Participants

Patients join research networks, grant consent, agree to be “sought” and to enroll – “on-demand” participants

Biospecimen Collections

Researchers can access and query large collections of well-characterized, clinically annotated specimens

Discovery of Correlations

Biomarkers are identified and validated; disease sub-groups emerge

Individualization of Treatment

Patients are identified by sub-groups and treated appropriately



Clinical Practice



Electronic Health Records

EHRs can connect to clinical trials in hospital settings



Research Finding Knowledgebases

Large-scale databases of latest research findings are connected to health delivery encounter

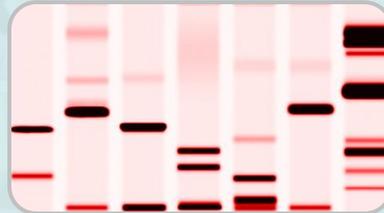


Learning Healthcare System

Local and national clinical encounter information is fed back to care providers to help inform clinical decision making



Consumer



My Genomic Profile

Consumers get their genetic and predisposition risk information



My Prevention Strategies

Consumers work with genetic counselors; coordinate with health care provider



My Clinical Record

Consumers link to their clinical histories with genetic profiles; access clinical research; participate in volunteer networks



Standards



Interoperability



Data Sharing



Connectivity

caGRID



Academic/Health Care Delivery

- Baylor College of Medicine
- Duke
- Georgetown
- Institute of Medicine
- NCCCP
- UCSF

Diagnostic

- Cellpoint
- Genzyme Genetics
- Monogram Biosciences

(Bio)Pharmaceutical

- Novartis
- Exelixis
- Genzyme
- J&J

IT/EHR/PHR

- Cerner
- Health IT Inc.
- Microsoft
- Oracle
- IBM

Foundations/Non-Profit/Advocacy

- Brookings Institution
- Canyon Ranch Institute
- CollabRx
- Critical Path Institute
- *FasterCures*
- Lance Armstrong Foundation
- Personalized Medicine Coalition

Health Care Consultancy

- Booz Allen Hamilton
- Feinstein Kean Healthcare
- Deliotte

Government

- CDC
- HHS Personalized Health Care Initiative
- NCI
- ONC

Payers

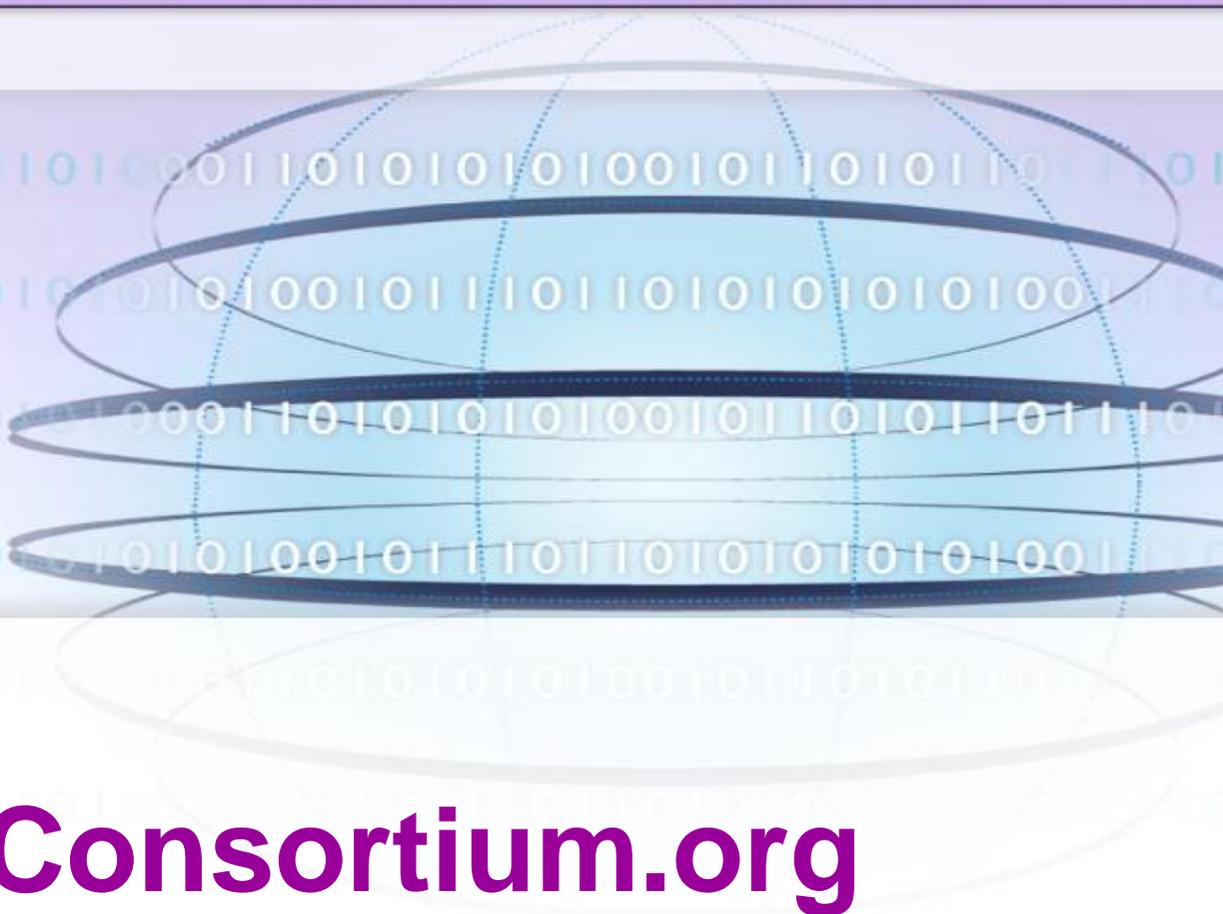
- Kaiser Permanente

Venture Capital

- Health Evolution Partners
- MDV

Personal Genomics

- Navigenics
- 23 and Me



BIGHEALTH
CONSORTIUM™

<http://BIGHealthConsortium.org>

Join the effort!!!

More information:
caBIG.cancer.gov

Join caBIG effort:
caBIG.nci.nih.gov

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